

CLAIMS

The invention is claimed as follows:

1. A method for treating infertility in a subject, the subject having a ratio of T helper 1 (Th1) immune response to T helper 2 (Th2) immune response, and the method comprises reducing the ratio of Th1 immune response to Th2 immune response in the subject to inhibit spontaneous abortion or implantation failure.
2. The method of claim 1, wherein the implantation failure occurs after assisted reproductive technology (ART) cycles.
3. The method of claim 2, wherein the ART is in vitro fertilization.
4. The method of claim 1, wherein the ratio of Th1 immune response to Th2 immune response in the subject is a ratio of absolute cell counts of a representative population of Th1 cells to a representative population of Th2 cells.
5. The method of claim 1, wherein the ratio of Th1 immune response to Th2 immune response in the subject is determined by measuring a ratio of the level of a Th1 cytokine to a Th2 cytokine.
6. The method of claim 5, wherein the levels of Th1 and Th2 cytokines are serum levels.
7. The method of claim 5, wherein the levels of Th1 and Th2 cytokines are intracellular levels.
8. The method of claim 1, wherein the method of reducing the ratio of Th1 immune response to Th2 immune response is to reduce the absolute counts of Th1 cells in the subject.
9. The method of claim 8, wherein the Th1 cell is a TNF- α expressing CD3+/CD4+ T-cell.
10. The method of claim 1, wherein the method of reducing the ratio of Th1 immune response to Th2 immune response is to increase the absolute counts of Th2 cells in the subject.
11. The method of claim 10, wherein the Th2 cell is an IL-4 expressing CD3+/CD8- T-cell.

12. The method of claim 1, wherein the method of reducing the ratio of Th1 immune response to Th2 immune response is to suppress the Th1 cytokines in the subject.
13. The method of claim 1, wherein the method of reducing the ratio of Th1 immune response to Th2 immune response is to enhance the level of Th2 cytokines in the subject.
14. The method of claim 12, wherein the Th1 cytokines are selected from the group consisting of IL-1, IL-2, TNF- α , and IFN- γ .
15. The method of claim 13, wherein the Th2 cytokines are selected from the group consisting of IL-4, IL-5, IL-6, IL-10.
16. The method of claim 5, wherein the Th1 to Th2 cytokine ratio is a ratio of IFN- γ to IL-4.
17. The method of claim 5, wherein the Th1 to Th2 cytokine ratio is a ratio of IFN- γ to IL-10.
18. The method of claim 5, wherein the Th1 to Th2 cytokine ratio is a ratio of TNF- α to IL-4.
19. The method of claim 5, wherein the Th1 to Th2 cytokine ratio is a ratio of TNF- α to IL-10.
20. The method of claim 5, wherein the method of reducing the count of Th1 cells is by administering an effective dose of an inhibitor of a costimulatory signal of a T-cell.
21. The method of claim 20, wherein the agent is an antibody to CD80.
22. The method of claim 20, wherein the agent is an antibody to CD86.
23. The method of claim 20, wherein the agent is an antibody to ICOS.
24. The method of claim 20, wherein the agent is a soluble form of CD28.
25. The method of claim 20, wherein the agent is a soluble form of ICOS.
26. The method of claim 20, wherein the agent is a soluble form of CTLA4.

27. The method of claim 10, wherein the method of increasing the count of Th2 cells is by administering an effective dose of a T helper 2-immuno-stimulatory nucleic acid.
28. The method of claim 12, wherein the method of suppressing the Th1 cytokines is by administering an effective dose of a Th1 cytokine antagonist to the subject.
29. The method of claim 28, wherein the Th1 cytokine antagonist is an inhibitor of the synthesis of the cytokine.
30. The method of claim 28, wherein the Th1 cytokine antagonist blocks the binding of the cytokine to its receptor.
31. The method of claim 28, wherein the Th1 cytokine antagonist inactivates the cytokine by binding to the cytokine.
32. The method of claim 28, wherein the Th1 cytokine antagonist is a polyclonal antibody.
33. The method of claim 28, wherein the Th1 cytokine antagonist is a monoclonal antibody.
34. The method of claim 28, wherein the Th1 cytokine antagonist is a soluble receptor of the cytokine.
35. The method of claim 28, wherein the Th1 cytokine antagonist is selected from the group consisting of: IL-1 antagonists, IL-2 antagonists, TNF- α antagonists, and IFN- γ antagonists.
36. The method of claim 35, wherein the TNF- α antagonist is infliximab.
37. The method of claim 35, wherein the TNF- α antagonist is etanercept.
38. The method of claim 35, wherein the TNF- α antagonist is D2E7.
39. The method of claim 35, wherein the TNF- α antagonist is CDP571.
40. The method of claim 35, wherein the TNF- α antagonist is CDP870.
41. The method of claim 35, wherein the TNF- α antagonist is a thalidomide analog.

42. The method of claim 35, wherein the TNF- α antagonist is a phosphodiesterase type IV inhibitor.
43. The method of claim 1, wherein the treatment of infertility further comprises enhancing embryo implantation, pregnancy, or birth rates of the subject.
44. The method of claim 1, wherein the treatment of infertility enhances the ability of the subject to carry at least one embryo to term.
45. The method of claim 1, wherein the subject is a human.
46. The method of claim 1, wherein the subject has had one or more previous spontaneous abortions or implantation failures.
47. The method of claim 46, wherein the implantation failures occur after ART cycles.
48. The method of claim 47, wherein the ART is in vitro fertilization.
49. The method of claim 1, wherein the subject undergoes natural conception.
50. The method of claim 1, wherein the subject undergoes ART cycles.
51. The method of claim 50, wherein the ART is in vitro fertilization.
52. The method of claim 1, wherein the subject undergoes ovulation induction cycles.
53. A method for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the method comprising administering a therapeutically effective dosage level of a TNF- α antagonist to the subject.
54. The method of claim 53, wherein the implantation failure occurs after ART cycles.
55. The method of claim 54, wherein the ART is in vitro fertilization.
56. The method of claim 53, further enhancing the ability of the subject to carry at least one embryo to term.
57. The method of claim 53, wherein the subject is a human.

58. The method of claim 53, wherein the subject has had one or more previous spontaneous abortions or implantation failures.
59. The method of claim 58, wherein the implantation failures occur after ART cycles.
60. The method of claim 59, wherein the ART is in vitro fertilization.
61. The method of claim 53, wherein the subject undergoes natural conception.
62. The method of claim 53, wherein the subject undergoes ART cycles.
63. The method of claim 62, wherein the ART is in vitro fertilization.
64. The method of claim 53, wherein the subject undergoes ovulation induction cycles.
65. The method of claim 53, wherein the TNF- α antagonist is infliximab.
66. The method of claim 53, wherein the TNF- α antagonist is etanercept.
67. The method of claim 53, wherein the TNF- α antagonist is D2E7.
68. The method of claim 53, wherein the TNF- α antagonist is CDP571.
69. The method of claim 53, wherein the TNF- α antagonist is CDP870.
70. The method of claim 53, wherein the TNF- α antagonist is a thalidomide analog.
71. The method of claim 53, wherein the TNF- α antagonist is a phosphodiesterase type IV inhibitor.
72. A pharmaceutical composition for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the composition comprising a TNF- α antagonist formulated in a formulation suitable for administration to the subject vaginally.
73. A method of enhancing the ability of a subject to carry at least one embryo to term comprising administering to the subject an effective dose of a TNF- α antagonist to inhibit TNF- α in the subject to inhibit spontaneous abortion or implantation failure..
74. The method of claim 73, wherein the implantation failure occurs after ART cycles.

75. The method of claim 74, wherein the ART is in vitro fertilization.
76. The method of claim 73, wherein the subject is a human.
77. The method of claim 73, wherein the subject has had one or more previous spontaneous abortions or implantation failures.
78. The method of claim 73, wherein the TNF- α antagonist is infliximab.
79. The method of claim 73, wherein the TNF- α antagonist is etanercept.
80. The method of claim 73, wherein the TNF- α antagonist is D2E7.
81. The method of claim 73, wherein the TNF- α antagonist is CDP571.
82. The method of claim 37, wherein the TNF- α antagonist is CDP870.
83. The method of claim 73, wherein the TNF- α antagonist is a thalidomide analog.
84. The method of claim 73, wherein the TNF- α antagonist is a phosphodiesterase type IV inhibitor.
85. A pharmaceutical composition for enhancing the ability of a subject to carry at least one embryo to term comprising a TNF- α antagonist to inhibit TNF- α in the subject to inhibit spontaneous abortion or implantation failure, wherein the TNF- α is formulated in formulation suitable for administration to the subject vaginally.
86. A method for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the method comprising administering a therapeutically effective dosage level of infliximab to the subject.
87. The method of claim 86, wherein the implantation failure occurs after ART cycles.
88. The method of claim 86, wherein the ART is in vitro fertilization.
89. The method of claim 86, further enhancing the ability of the subject to carry at least one embryo to term.
90. The method of claim 86, wherein the subject is a human.

91. The method of claim 86, wherein the subject has had one or more previous spontaneous abortions or implantation failures.
92. The method of claim 91, wherein the implantation failures occur after ART cycles.
93. The method of claim 92, wherein the ART is in vitro fertilization.
94. The method of claim 86, wherein the subject undergoes natural conception.
95. The method of claim 86, wherein the subject undergoes ART cycles.
96. The method of claim 95, wherein the ART is in vitro fertilization.
97. The method of 86, wherein the subject undergoes ovulation induction cycles.
98. The method of claim 86, wherein the therapeutically effective dosage level of infliximab is from about 3 mg/Kg to about 10 mg/Kg.
99. The method of claim 86, wherein the administration of infliximab is performed by delivering a therapeutically effective dosage level of infliximab intravenously.
100. The method of claim 86, wherein the administration of infliximab is performed by delivering a therapeutically effective dosage level of infliximab subcutaneously.
101. The method of claim 86, wherein the administration of infliximab is performed by delivering a therapeutically effective dosage level of infliximab vaginally.
102. The method of claim 101, wherein the infliximab is in a gel form.
103. The method of claim 86, wherein the administration of infliximab is performed by delivering a therapeutically effective dosage of infliximab at least once prior to index conception cycle day one.
104. The method of claim 86, wherein the step of the administration of infliximab is performed by delivering a therapeutically effective dosage of infliximab at least once on index conception cycle day one.

105. The method of claim 86, wherein the administration of infliximab is performed by delivering a therapeutically effective dosage of infliximab at least once after index conception cycle day one.
106. The method of claim 86, wherein the subject further receives lymphocyte immunization or autoimmune treatment.
107. The method of claim 86, wherein the subject further receives intravenous immunoglobulin G.
108. The method of claim 86, wherein the subject further receives at least one anticoagulant.
109. The method of claim 108, wherein one of the anticoagulants is heparin.
110. The method of claim 108, wherein one of the anticoagulants is aspirin.
111. The method of claim 86, wherein the subject further receives prednisone.
112. A pharmaceutical composition for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the composition comprising infliximab formulated in a formulation suitable for administration to the subject vaginally.
113. A method for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the method comprising administering a therapeutically effective dosage level of etanercept to the subject.
114. The method of claim 113, wherein the implantation failure occurs after ART cycles.
115. The method of claim 114, wherein the ART is in vitro fertilization
116. The method of claim 113, further enhancing the ability of the subject to carry at least one embryo to term.
117. The method of claim 113, wherein the subject is a human.
118. The method of claim 113, wherein the subject has had one or more previous spontaneous abortions or implantation failures.

119. The method of claim 118, wherein the implantation failures occur after ART cycles.
120. The method of claim 119, wherein the ART is in vitro fertilization.
121. The method of claim 113, wherein the subject undergoes natural conception.
122. The method of claim 113, wherein the subject undergoes ART cycles.
123. The method of claim 122, wherein the ART is in vitro fertilization.
124. The method of claim 113, wherein the subject undergoes ovulation induction cycles.
125. The method of claim 113, wherein the therapeutically effective dosage level of etanercept is from about 3 mg to about 50 mg.
126. The method of claim 113, where the administration of etanercept is performed by delivering a therapeutically effective dosage level of etanercept subcutaneously.
127. The method of claim 113, wherein the administration of etanercept is performed by delivering a therapeutically effective dosage level of etanercept vaginally.
128. The method of claim 127, wherein the etanercept is in a gel form.
129. The method of claim 113, wherein the administration of etanercept is performed by delivering a therapeutically effective dosage of etanercept at least once prior to index conception cycle day one.
130. The method of claim 113, wherein the administration of etanercept is performed by delivering a therapeutically effective dosage of etanercept at least once on index conception cycle day one.
131. The method of claim 113, wherein the administration of etanercept is performed by delivering a therapeutically effective dosage of etanercept at least once after index conception cycle day one.
132. The method of claim 113, wherein the subject further receives lymphocyte immunization or autoimmune treatment.

133. The method of claim 113, wherein the subject further receives intravenous immunoglobulin G.
134. The method of claim 113, wherein the subject further receives at least one anticoagulant.
135. The method of claim 134, wherein one of the anticoagulants is heparin.
136. The method of claim 134, wherein one of the anticoagulants is aspirin.
137. The method of claim 113, wherein the subject further receives prednisone.
138. A pharmaceutical composition for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the composition comprising etanercept formulated in a formulation suitable for administration to the subject vaginally.
139. A method for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the method comprising administering a therapeutically effective dosage level of D2E7 to the subject.
140. The method of claim 139, wherein the implantation failure occurs after ART cycles.
141. The method of claim 140, wherein the ART is in vitro fertilization.
142. The method of claim 139, further enhancing the ability of the subject to carry at least one embryo to term.
143. The method of claim 139, wherein the subject is a human.
144. The method of claim 139, wherein the subject has had one or more previous spontaneous abortions or implantation failures.
145. The method of claim 144, wherein the implantation failures occur after ART cycles.
146. The method of claim 145, wherein the ART is in vitro fertilization.
147. The method of claim 139, wherein the subject undergoes natural conception.
148. The method of claim 139, wherein the subject undergoes ART cycles.

149. The method of claim 148, wherein the ART is in vitro fertilization.
150. The method of claim 139, wherein the subject undergoes ovulation induction cycles.
151. The method of claim 124, wherein the dosage level of D2E7 is from about 5 mg to about 50 mg.
152. The method of claim 139, wherein the administration of D2E7 is performed by delivering a therapeutically effective dosage level of D2E7 subcutaneously.
153. The method of claim 139, wherein the administration of D2E7 is performed by delivering a therapeutically effective dosage level of D2E7 intravenously.
154. The method of claim 139, wherein the administration of D2E7 is performed by delivering a therapeutically effective dosage level of D2E7 vaginally.
155. The method of claim 139, wherein the administration of D2E7 is performed by delivering a therapeutically effective dosage of D2E7 at least once prior to index conception cycle day one.
156. The method of claim 139, wherein the administration of D2E7 is performed by delivering a therapeutically effective dosage of D2E7 at least once on index conception cycle day one.
157. The method of claim 139, wherein the administration of D2E7 is performed by delivering a therapeutically effective dosage of D2E7 at least once after index conception cycle day one.
158. The method of claim 139, wherein the subject further receives lymphocyte immunization or autoimmune treatment.
159. The method of claim 139, wherein the subject further receives intravenous immunoglobulin G.
160. The method of claim 139, wherein the subject further receives at least one anticoagulant.
161. The method of claim 160, wherein one of the anticoagulants is heparin.

162. The method of claim 160, wherein one of the anticoagulants is aspirin.
163. The method of claim 139, wherein the subject further receives prednisone.
164. A pharmaceutical composition for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the composition comprising D2E7 formulated in a formulation suitable for administration to the subject vaginally.
165. A method for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the method comprising administering a therapeutically effective dosage level of CDP571 to the subject.
166. The method of claim 165, wherein the implantation failure occurs after ART cycles.
167. The method of claim 166, wherein the ART is in vitro fertilization.
168. The method of claim 165, further enhancing the ability of the subject to carry at least one embryo to term.
169. The method of claim 165, wherein the subject is a human.
170. The method of claim 165, wherein the subject has had one or more previous spontaneous abortions, or implantation failures.
171. The method of claim 170, wherein the implantation failures occur after ART cycles.
172. The method of claim 171, wherein the ART is in vitro fertilization.
173. The method of claim 170, wherein the subject undergoes natural conception.
174. The method of claim 165, wherein the administration of CDP571 is performed by delivering a therapeutically effective dosage level of CDP571 subcutaneously.
175. The method of claim 165, wherein the administration of CDP571 is performed by delivering a therapeutically effective dosage level of CDP571 vaginally.
176. A pharmaceutical composition for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy,

or birth rates, the composition comprising CDP571 formulated in a formulation suitable for administration to the subject vaginally.

177. A method for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the method comprising administering a therapeutically effective dosage level of CDP870 to the subject.

178. The method of claim 177, wherein the implantation failure occurs after ART cycles.

179. The method of claim 178, wherein the ART is in vitro fertilization.

180. The method of claim 177, further enhancing the ability of the subject to carry at least one embryo to term.

181. The method of claim 177, wherein the subject is a human.

182. The method of claim 177, wherein the subject has had one or more previous spontaneous abortions or implantation failures.

183. The method of claim 177, wherein the subject undergoes natural conception.

184. The method of claim 182, wherein the implantation failures occur after ART cycles.

185. The method of claim 184, wherein the ART is in vitro fertilization.

186. The method of claim 177, wherein the administration of CDP870 is performed by delivering a therapeutically effective dosage level of CDP870 subcutaneously.

187. The method of claim 177, wherein the administration of CDP870 is performed by delivering a therapeutically effective dosage level of CDP870 vaginally.

188. A pharmaceutical composition for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the composition comprising CDP870 formulated in a formulation suitable for administration to the subject vaginally.

189. A method for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the method

comprising administering a therapeutically effective dosage level of a thalidomide analog to the subject.

190. The method of claim 189, wherein the implantation failure occurs after ART cycles.

191. The method of claim 190, where in the ART is in vitro fertilization

192. The method of claim 189, further enhancing the ability of the subject to carry at least one embryo to term.

193. The method of claim 189, wherein the subject is a human.

194. The method of claim 189, wherein the subject undergoes natural conception.

195. The method of claim 189, wherein the subject has had one or more previous spontaneous abortions or implantation failures.

196. The method of claim 194, wherein the implantation failures occur after ART cycles.

197. The method of claim 196, wherein the ART is in vitro fertilization.

198. The method of claim 189, wherein the administration of the thalidomide analog is performed by delivering a therapeutically effective dosage level of the thalidomide analog orally, vaginally, subcutaneously or intravenously.

199. The method of claim 189, wherein the administration of the thalidomide analog is performed subcutaneously in the woman wherein the dosage level is from about 50 mg/Kg to about 800 mg/Kg.

200. The method of claim 189, wherein the therapeutically effective dosage level is sufficient to produce a blood level of the thalidomide analog of at least 0.1 µg/ml.

201. A pharmaceutical composition for treating infertility in a subject by inhibiting spontaneous abortion or implantation failures for enhancing embryo implantation, pregnancy, or birth rates, the composition comprising a thalidomide analog formulated in a formulation suitable for administration to the subject vaginally.

202. A method for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the method

comprising administering a therapeutically effective dosage level of a phosphodiesterase type IV inhibitor to the subject.

203. The method of claim 202, wherein the implantation failure occurs after ART cycles.

204. The method of claim 203, wherein the ART is in vitro fertilization cycles.

205. The method of claim 202, further enhancing the ability of the subject to carry at least one embryo to term.

206. The method of claim 202, wherein the subject undergoes natural conception.

207. The method of claim 202, wherein the subject is a human.

208. The method of claim 202, wherein the subject has had one or more previous spontaneous abortions or implantation failures.

209. The method of claim 208, wherein implantation failures occur after ART cycles.

210. The method of claim 209, wherein the ART is in vitro fertilization.

211. A pharmaceutical composition for treating infertility in a subject by inhibiting spontaneous abortion or implantation failure for enhancing embryo implantation, pregnancy, or birth rates, the composition comprising a phosphodiesterase type IV inhibitor formulated in a formulation suitable for administration to the subject vaginally.

212. A method for diagnosing infertility in a subject with recurrent spontaneous abortions or one or more implantation failures comprising determining a ratio of Th1 and Th2 immune responses of the subject and comparing the ratio with that from subjects with normal pregnancies to determine if the subject is at risk of infertility or if the subject is suitable for treatment of the infertility by reducing ratio of Th1 to Th2 immune responses in the subject.

213. The method of claim 212, wherein the implantation failures occur after ART cycles.

214. The method of claim 213, wherein the ART is in vitro fertilization.

215. The method of claim 212, wherein the Th1 immune response is measured by the absolute cell counts of Th1 cytokine expressing T-cells, and the Th2 immune response is measured by the absolute cell counts of Th2 cytokine expressing T-cells.

216. The method of claim 215, wherein the Th1 and Th2 immune responses are measured by flow cytometry analysis.
217. The method of claim 215, wherein the Th1 cytokine expressing T-cell is a TNF- α expressing CD3+/CD4+ T-cell.
218. The method of claim 215, wherein the Th2 cytokine expressing T-cell is a IL-4 expressing CD3+/CD4+ T-cell.
219. The method of claim 212, wherein the ratio of Th1 immune response to Th2 immune response is a ratio of the levels of Th1 and Th2 cytokines.
220. The method of claim 219, wherein the levels of Th1 and Th2 cytokines are serum levels.
221. The method of claim 219, wherein the levels of Th1 and Th2 cytokines are intracellular levels.
222. The method of claim 219, wherein the Th1 cytokine is IL-1.
223. The method of claim 219, wherein the Th1 cytokine is IL-2.
224. The method of claim 219, wherein the Th1 cytokine is TNF- α .
225. The method of claim 219, wherein the Th1 cytokine is IFN- γ .
226. The method of claim 219, wherein the Th2 cytokine is IL-4.
227. The method of claim 219, wherein the Th2 cytokine is IL-5.
228. The method of claim 219, wherein the Th2 cytokine is IL-6.
229. The method of claim 219, wherein the Th2 cytokine is IL-10.
230. The method of claim 219, wherein the Th1 to Th2 cytokine ratio is the ratio of IFN- γ to IL-4.
231. The method of claim 219, wherein the Th1 to Th2 cytokine ratio is the ratio of IFN- γ to IL-10.

232. The method of claim 219, wherein the Th1 to Th2 cytokine ratio is the ratio of TNF- α to IL-4.

233. The method of claim 219, wherein the Th1 to Th2 cytokine ratio is the ratio of TNF- α to IL-10.

234. A diagnostic kit for diagnosing infertility with recurrent spontaneous abortions or one or more implantation failure in a subject, the kit comprising:

- (a) means for determining Th1 immune response; and
- (b) means for determining Th2 immune response.

235. The diagnostic kit of claim 234, wherein the implantation failures occur after ART cycles.

236. The diagnostic kit of claim 235, wherein the ART is in vitro fertilization.

237. The diagnostic kit of claim 234, further providing a ratio of Th1 to Th2 immune responses in a population of other subjects with normal pregnancies.

238. The diagnostic kit of claim 234, wherein the Th1 immune response is the levels of Th1 cytokines in the subject, the means for determining the Th1 immune response comprises a Th1 cytokine antibody, the Th2 immune response is the levels of Th2 cytokines in the subject, and the means for determining the Th2 immune response comprises a Th2 cytokine antibody.

239. The diagnostic kit of claim 234, wherein the antibody is a polyclonal or monoclonal antibody or a fragment thereof.

240. A method for determining whether a treatment of infertility in a subject with recurrent spontaneous abortions or one or more implantation failures by reducing the ratio of Th1 to Th2 immune responses is having the desired effect of enhancing embryo implantation, pregnancy, or birth rates in the subject, the method comprising the steps of:

- (a) determining the ratio of the level of Th1 immune response to the level of Th2 immune response of the subject before the treatment;
- (b) determining the ratio of the level of Th1 immune response to the level of Th2 immune response of the subject after the treatment;

- (c) determining whether the ratio of Th1 to Th2 immune responses in the subject after the treatment is lower than that in the subject before the treatment to determine if the treatment has the desired effect.
241. The method of claim 240, wherein the implantation failures occur after ART cycles.
242. The method of claim 241, wherein the ART is in vitro fertilization.
243. The method of claim 240, wherein the Th1 immune response is measured by the absolute cell counts of Th1 cytokine expressing T-cells and the Th2 immune response is measured by the absolute cell counts of Th2 cytokine expressing T-cells.
244. The method of claim 243, wherein the Th1 and Th2 immune responses are measured by flow cytometry analysis.
245. The method of claim 243, wherein the Th1 cytokine expressing T-cell is a TNF- α expressing CD3+/CD4+ T-cell.
246. The method of claim 243, wherein the Th2 cytokine expressing T-cell is a IL-4 expressing CD3+/CD4+ T-cell.
247. The method of claim 243, wherein the ratio of Th1 immune response to Th2 immune response is a ratio of the level of Th1 and Th2 cytokines.
248. The method of claim 247, wherein the levels of Th1 and Th2 cytokines are serum levels.
249. The method of claim 247, wherein the levels of Th1 and Th2 cytokines are intracellular levels.
250. The method of claim 247, wherein the Th1 cytokine is IL-1.
251. The method of claim 247, wherein the Th1 cytokine is IL-2.
252. The method of claim 247, wherein the Th1 cytokine is TNF- α .
253. The method of claim 247, wherein the Th1 cytokine is IFN- γ .
254. The method of claim 247, wherein the Th2 cytokine is IL-4.

255. The method of claim 247, wherein the Th2 cytokine is IL-5.
256. The method of claim 247, wherein the Th2 cytokine is IL-6.
257. The method of claim 247, wherein the Th2 cytokine is IL-10.
258. A diagnostic method for determining whether a TNF- α antagonist therapy will likely enhance embryo implantation, pregnancy, or birth rates in a subject with recurrent spontaneous abortions or one or more implantation failures, the method comprising:
- (a) measuring a level of TNF- α in the subject;
 - (b) determining whether the level of TNF- α in the subject is higher than that in other subjects with normal pregnancies.
259. The method of claim 258, wherein the implantation failures occur after ART cycles.
260. The method of claim 259, wherein the ART is in vitro fertilization.
261. The method of claim 258, wherein the level of TNF- α is determined by a method using a TNF- α antibody.
262. The method of claim 261, wherein the antibody is a polyclonal or monoclonal antibody or a fragment thereof.
263. The method of claim 258, wherein the level of TNF- α is serum level.
264. The method of claim 263, wherein the serum level of TNF- α of the subject is considered higher than the level in other subjects with normal pregnancies when the level in the subject is higher than 12 pg/ml.
265. The method of claim 258, wherein the level of TNF- α is intracellular level.
266. A diagnostic kit of claim 258, comprising a means for measuring the level of TNF- α .
267. The diagnostic kit of claim 266, wherein the means for measuring the level of TNF- α is an antibody.
268. The diagnostic kit of claim 267, wherein the antibody is a polyclonal or a monoclonal antibody or a fragment thereof.

269. A method for determining whether a TNF- α antagonist treatment of infertility in a subject with recurring spontaneous abortions or one or more implantation failures is having the desired effect of enhancing embryo implantation, pregnancy, or birth rates in the subject, the method comprising the steps of:

- (a) measuring the level of TNF- α in the subject before the TNF- α antagonist treatment;
- (b) measuring the level of TNF- α in the subject after the TNF- α antagonist treatment;
- (c) determining whether the level of TNF- α in the subject after the TNF- α antagonist treatment is lower than that in the subject before the treatment.

270. The method of claim 269, wherein the implantation failures occur after ART cycles.

271. The method of claim 270, wherein the ART is in vitro fertilization.

272. The method of claim 269, wherein the level of TNF- α is serum level.

273. The method of claim 269, wherein the level of TNF- α is intracellular level.

274. A diagnostic kit of claim 269, comprising a means for measuring the level of TNF- α .

275. The diagnostic kit of claim 274, wherein the means for measuring the level of TNF- α is an antibody.

276. The diagnostic kit of claim 275, wherein the antibody is a polyclonal or monoclonal antibody or a fragment thereof.